

# SEQUENCE LISTING

<110> Sharma et al.

<120> SOLUBLE NOTCH-BASED SUBSTRATES FOR GAMMA SECRETASE AND METHODS AND COMPOSITIONS FOR USING SAME

<130> 28341/01130

<160> 17

<170> PatentIn version 3.1

<210> 1

<211> 2190

<212> DNA

<213> Artificial sequence

<220>

<223> DNA encoding synthetic fusion of notch and nus

<400> 1

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Thr Ala Thr Lys Lys Lys Tyr Glu Gln Glu Ile Asp Val Arg Val Gln  
35 40 45

Ile Asp Arg Lys Ser Gly Asp Phe Asp Thr Phe Arg Arg Trp Leu Val  
50 55 60

Val Asp Glu Val Thr Gln Pro Thr Lys Glu Ile Thr Leu Glu Ala Ala  
65 70 75 80

Arg Tyr Glu Asp Glu Ser Leu Asn Leu Gly Asp Tyr Val Glu Asp Gln  
85 90 95

Ile Glu Ser Val Thr Phe Asp Arg Ile Thr Thr Gln Thr Ala Lys Gln  
100 105 110

Val Ile Val Gln Lys Val Arg Glu Ala Glu Arg Ala Met Val Val Asp  
115 120 125

Gln Phe Arg Glu His Glu Gly Glu Ile Ile Thr Gly Val Val Lys Lys  
130 135 140

Val Asn Arg Asp Asn Ile Ser Leu Asp Leu Gly Asn Asn Ala Glu Ala  
145 150 155 160

Val Ile Leu Arg Glu Asp Met Leu Pro Arg Glu Asn Phe Arg Pro Gly  
165 170 175

Asp Arg Val Arg Gly Val Leu Tyr Ser Val Arg Pro Glu Ala Arg Gly  
180 185 190

Ala Gln Leu Phe Val Thr Arg Ser Lys Pro Glu Met Leu Ile Glu Leu  
195 200 205

Phe Arg Ile Glu Val Pro Glu Ile Gly Glu Glu Val Ile Glu Ile Lys  
210 215 220

Ala Ala Ala Arg Asp Pro Gly Ser Arg Ala Lys Ile Ala Val Lys Thr

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	260	265	270			
Ile Val Leu Trp	Asp Asp Asn Pro Ala Gln Phe Val	Ile Asn Ala Met				
	275	280	285			
Ala Pro Ala Asp	Val Ala Ser Ile Val Val Asp	Glu Asp Lys His Thr				
	290	295	300			
Met Asp Ile Ala	Val Glu Ala Gly Asn Leu Ala Gln Ala	Ile Gly Arg				
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Asn Gly Gln Asn	Val Arg Leu Ala Ser Gln	Leu Ser Gly Trp Glu Leu				
	325	330	335			
Asn Val Met Thr	Val Asp Asp Leu Gln Ala Lys His Gln	Ala Glu Ala				
	340	345	350			
His Ala Ala Ile	Asp Thr Phe Thr Lys Tyr Leu Asp	Ile Asp Glu Asp				
	355	360	365			
Phe Ala Thr Val	Leu Val Glu Glu Gly Phe Ser Thr	Leu Glu Glu Leu				
	370	375	380			
Ala Tyr Val Pro	Met Lys Glu Leu Leu Glu Ile	Glu Gly Leu Asp Glu				
385	390	395	400			
Pro Thr Val Glu	Ala Leu Arg Glu Arg Ala Lys Asn Ala	Leu Ala Thr				
	405	410	415			
Ile Ala Gln Ala	Gln Glu Glu Ser Leu Gly Asp Asn Lys	Pro Ala Asp				
	420	425	430			
Asp Leu Leu Asn	Leu Glu Gly Val Asp Arg Asp Leu	Ala Phe Lys Leu				
	435	440	445			
Ala Ala Arg Gly	Val Cys Thr Leu Glu Asp Leu Ala	Glu Gln Gly Ile				
	450	455	460			
Asp Asp Leu Ala	Asp Ile Glu Gly Leu Thr Asp	Glu Lys Ala Gly Ala				
465	470	475	480			
Leu Ile Met Ala	Ala Arg Asn Ile Cys Trp Phe Gly Asp	Glu Ala Thr				
	485	490	495			
Ser Gly Ser Gly	His His His His His His Ser Ala Gly	Lys Glu Thr				
	500	505	510			
Ala Ala Ala Lys	Phe Glu Arg Gln His Met Asp Ser	Pro Pro Pro Thr				
	515	520	525			
Gly Leu Val Pro	Arg Gly Ser Ala Gly Ser Gly Thr	Ile Asp Asp Asp				
	530	535	540			
Asp Lys Ser Pro	Gly Ala Arg Gly Ser Glu Phe Asn Ile	Pro Tyr Lys				
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Ile Glu Ala Val Lys Ser Glu Pro Val Glu Pro Pro Leu Pro Ser Gln  
565 570 575

Leu His Leu Met Tyr Val Ala Ala Ala Phe Val Leu Leu Phe Phe  
580 585 590

Val Gly Cys Gly Val Leu Leu Ser Arg Lys Arg Arg Arg Gln His Gly  
595 600 605

Gln Leu Trp Phe Pro Glu Gly Phe Lys Val Ser Glu Ala Ser Lys Lys  
610 615 620

Lys Arg Arg Glu Pro Leu Gly Glu Asp Ser Val Gly Leu Lys Pro Leu  
625 630 635 640

Lys Asn Ala Ser Asp Gly Ala Leu Met Asp Asp Asn Gln Asn Glu Trp  
645 650 655

Gly Asp Glu Asp Leu Glu Thr Lys Lys Phe Arg Phe Glu Glu Pro Val  
660 665 670

Val Leu Pro Asp Leu Ser Asp Gln Thr Asp His Arg Gln Trp Thr Gln  
675 680 685

Gln His Leu Asp Ala Ala Asp Leu Arg Met Ser Ala Met Ala Pro Thr  
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Pro Pro Gln Gly Glu Val Asp Ala Asp Asp Tyr Lys Asp Asp Asp Asp  
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Lys His His His His His His His His  
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gggggtgctgc tgtcccgcga gcgccggcgg cagcatggcc agctctggtt ccctgagggt 180  
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<223> Wildtype notch protein sequence

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 35 40 45  
 Arg Arg Gln His Gly Gln Leu Trp Phe Pro Glu Gly Phe Lys Val Ser  
 50 55 60  
 Glu Ala Ser Lys Lys Lys Arg Arg Glu Pro Leu Gly Glu Asp Ser Val  
 65 70 75 80  
 Gly Leu Lys Pro Leu Lys Asn Ala Ser Asp Gly Ala Leu Met Asp Asp  
 85 90 95  
 Asn Gln Asn Glu Trp Gly Asp Glu Asp Leu Glu Thr Lys Lys Phe Arg  
 100 105 110  
 Phe Glu Glu Pro Val Val Leu Pro Asp Leu Ser Asp Gln Thr Asp His  
 115 120 125  
 Arg Gln Trp Thr Gln Gln His Leu Asp Ala Ala Asp Leu Arg Met Ser  
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 35 40 45  
 Ser Gly Ser Phe Val Gly Gln Arg Cys Gln Asp Pro Asn Pro Cys Leu  
 50 55 60  
 Ser Thr Arg Cys Lys Asn Ala Gly Thr Cys Tyr Val Val Asp His Gly  
 65 70 75 80  
 Gly Ile Val Asp Tyr Ala Cys Ser Cys Pro Leu Gly Phe Ser Gly Pro  
 85 90 95  
 Leu Cys Leu Thr Pro Leu Asp Lys Pro Cys Leu Ala Asn Pro Cys Arg  
 100 105 110  
 Asn Gly Gly Thr Cys Asp Leu Leu Thr Leu Thr Glu Tyr Lys Cys Arg  
 115 120 125

Cys Ser Pro Gly Trp Ser Gly Lys Ser Cys Gln Gln Ala Asp Pro Cys  
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 Ala Ser Asn Pro Cys Ala Asn Gly Gly Gln Cys Leu Pro Phe Glu Ser  
 145 150 155 160  
 Ser Tyr Ile Cys Arg Cys Pro Pro Gly Phe His Gly Pro Thr Cys Arg  
 165 170 175  
 Gln Asp Val Asn Glu Cys Ser Gln Asn Pro Gly Leu Cys Arg His Gly  
 180 185 190  
 Gly His Cys His Asn Glu Ile Gly Ser Tyr Arg Cys Ala Cys Cys Ala  
 195 200 205  
 Thr His Thr Gly Pro His Cys Glu Leu Pro Tyr Val Pro Cys Ser Pro  
 210 215 220  
 Ser Pro Cys Gln Asn Gly Ala Thr Cys Arg Pro Thr Gly Asp Thr Thr  
 225 230 235 240  
 His Glu Cys Ala Cys Leu Pro Gly Phe Ala Gly Gln Asn Cys Glu Glu  
 245 250 255  
 Asn Val Asp Asp Cys Pro Gly Asn Asn Cys Lys Asn Gly Gly Ala Cys  
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 Val Asp Gly Val Asn Thr Tyr Asn Cys Arg Cys Pro Pro Glu Val Thr  
 275 280 285  
 Gly Gln Tyr Cys Thr Glu Asp Val Asp Glu Cys Gln Leu Met Pro Asn  
 290 295 300  
 Ala Cys Gln Asn Ala Gly Thr Cys His Asn Thr His Gly Gly Tyr Asn  
 305 310 315 320  
 Cys Val Cys Val Asn Gly Trp Thr Gly Glu Asp Cys Ser Glu Asn Ile  
 325 330 335  
 Asp Asp Cys Ala Ser Ala Ala Cys Phe Gln Gly Ala Thr Cys His Asp  
 340 345 350  
 Arg Val Ala Ser Phe Tyr Cys Glu Cys Pro His Gly Arg Thr Gly Leu  
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 Leu Cys His Leu Lys His Ala Cys Ile Ser Asn Pro Cys Asn Glu Gly  
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 Ser Asn Cys Asp Thr Asn Pro Val Asn Gly Lys Arg Ile Cys Thr Cys  
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 Pro Ser Gly Tyr Thr Gly Pro Ala Cys Ser Gln Asp Val Asp Glu Cys  
 405 410 415  
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 420 425 430  
 Leu Gly Ser Phe Glu Cys Gln Cys Leu Gln Gly Tyr Thr Gly Pro Gly  
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Cys Glu Ile Asp Val Asn Glu Cys Ile Ser Asn Pro Cys Gln Asn Asp  
 450 455 460  
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 465 470 475 480  
 Gly Tyr Glu Gly Val Tyr Cys Glu Ile Asn Thr Asp Glu Cys Ala Ser  
 485 490 495  
 Ser Pro Cys Leu His Asn Gly His Cys Met Asp Lys Ile His Glu Phe  
 500 505 510  
 Gln Cys Gln Cys Pro Lys Gly Phe Asn Gly His Leu Cys Gln Tyr Asp  
 515 520 525  
 Val Asp Glu Cys Ala Ser Thr Pro Cys Lys Asn Gly Ala Lys Cys Leu  
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 Pro Gly Tyr Thr Gly His His Cys Glu Thr Asn Ile Asn Glu Cys His  
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 Ser Gln Pro Cys Arg His Gly Gly Thr Cys Gln Asp Arg Asp Asn Ser  
 610 615 620  
 Tyr Leu Cys Leu Cys Leu Lys Gly Thr Thr Gly Pro Asn Cys Glu Ile  
 625 630 635 640  
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 645 650 655  
 Asp Lys Ile Asp Gly Tyr Glu Cys Ala Cys Glu Pro Gly Tyr Thr Gly  
 660 665 670  
 Ser Met Cys Asn Val Asn Ile Asp Glu Cys Ala Gly Ser Pro Cys His  
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 Tyr Lys Cys Asp Cys Ala Pro Gly Trp Ser Gly Thr Asn Cys Asp Ile  
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 Leu Asn Gln Gly Thr Cys Ile Asp Asp Val Ala Gly Tyr Lys Cys Asn  
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 Cys Pro Leu Pro Tyr Thr Gly Ala Thr Cys Glu Val Val Leu Ala Pro  
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 850 855 860  
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 Pro Asn Pro Cys His Asn Gly Gly Ser Cys Thr Asp Gly Ile Asn Thr  
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 Lys Asn Gly Gly Arg Cys Trp Gln Thr Asn Thr Gln Tyr His Cys  
 1070 1075 1080  
 Glu Cys Arg Ser Gly Trp Thr Gly Val Asn Cys Asp Val Leu Ser  
 1085 1090 1095



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 His Tyr Cys His Cys Gln Ala Gly Tyr Thr Gly Ser Tyr Cys Glu  
 1130 1135 1140  
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 1160 1165 1170  
 Gly Tyr His Gly Ser Asn Cys Ser Glu Glu Ile Asn Glu Cys Leu  
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 Ser Gln Pro Cys Gln Asn Gly Gly Thr Cys Ile Asp Leu Thr Asn  
 1190 1195 1200  
 Ser Tyr Lys Cys Ser Cys Pro Arg Gly Thr Gln Gly Val His Cys  
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Cys Leu Cys Pro Ala Lys Phe Asn Gly Leu Leu Cys His Ile Leu  
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Arg Glu 1775	Pro	Leu	Gly	Glu	Asp 1780	Ser	Val	Gly	Leu	Lys 1785	Pro	Leu	Lys
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Gly Asp 1805	Glu	Asp	Leu	Glu	Thr 1810	Lys	Lys	Phe	Arg	Phe 1815	Glu	Glu	Pro
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Glu Asp 1895	Ala	Pro	Ala	Val	Ile 1900	Ser	Asp	Phe	Ile	Tyr 1905	Gln	Gly	Ala
Ser Leu 1910	His	Asn	Gln	Thr	Asp 1915	Arg	Thr	Gly	Glu	Thr 1920	Ala	Leu	His
Leu Ala 1925	Ala	Arg	Tyr	Ser	Arg 1930	Ser	Asp	Arg	Arg	Lys 1935	Arg	Leu	Glu
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Gly Thr 1985	Thr	Pro	Leu	Ile	Leu 1990	Ala	Ala	Arg	Leu	Ala 1995	Val	Glu	Gly
Met Leu 2000	Glu	Asp	Leu	Ile	Asn 2005	Ser	His	Ala	Asp	Val 2010	Asn	Ala	Val
Asp Asp 2015	Leu	Gly	Lys	Ser	Ala 2020	Leu	His	Trp	Ala	Ala 2025	Ala	Val	Asn

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Arg Arg 2060	Glu Ser Tyr Glu Thr 2065	Ala Lys Val Leu Leu 2070	Asp His Phe
Ala Asn 2075	Arg Asp Ile Thr Asp 2080	His Met Asp Arg Leu 2085	Pro Arg Asp
Ile Ala 2090	Gln Glu Arg Met His 2095	His Asp Ile Val Arg 2100	Leu Leu Asp
Glu Tyr 2105	Asn Leu Val Arg Ser 2110	Pro Gln Leu His Gly 2115	Thr Ala Leu
Gly Gly 2120	Thr Pro Thr Leu Ser 2125	Pro Thr Leu Cys Ser 2130	Pro Asn Gly
Tyr Pro 2135	Gly Asn Leu Lys Ser 2140	Ala Thr Gln Gly Lys 2145	Lys Ala Arg
Lys Pro 2150	Ser Thr Lys Gly Leu 2155	Ala Cys Gly Ser Lys 2160	Glu Ala Lys
Asp Leu 2165	Lys Ala Arg Arg Lys 2170	Ser Ser Gln Asp Gly 2175	Lys Gly Trp
Leu Leu 2180	Asp Ser Ser Ser Ser 2185	Met Leu Ser Pro Val 2190	Asp Ser Leu
Glu Ser 2195	Pro His Gly Tyr Leu 2200	Ser Asp Val Ala Ser 2205	His Pro Leu
Leu Pro 2210	Ser Pro Phe Gln Gln 2215	Ser Pro Ser Met Pro 2220	Leu Ser His
Leu Pro 2225	Gly Met Pro Asp Thr 2230	His Leu Gly Ile Ser 2235	His Leu Asn
Val Ala 2240	Ala Lys Pro Glu Met 2245	Ala Ala Leu Ala Gly 2250	Gly Ser Arg
Leu Ala 2255	Phe Glu His Pro Pro 2260	Pro Arg Leu Ser His 2265	Leu Pro Val
Ala Ser 2270	Ser Ala Cys Thr Val 2275	Leu Ser Thr Asn Gly 2280	Thr Gly Ala
Met Asn 2285	Phe Thr Val Gly Ala 2290	Pro Ala Ser Leu Asn 2295	Gly Gln Cys
Glu Trp 2300	Leu Pro Arg Leu Gln 2305	Asn Gly Met Val Pro 2310	Ser Gln Tyr
Asn Pro 2315	Leu Arg Pro Gly Val 2320	Thr Pro Gly Thr Leu 2325	Ser Thr Gln

Ala Ala Gly Leu Gln His Ser Met Met Gly Pro Leu His Ser Ser  
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 Leu Ser Thr Asn Thr Leu Ser Pro Ile Ile Tyr Gln Gly Leu Pro  
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 Gln Glu Ser Gln Ala Leu Pro Thr Ser Leu Pro Ser Ser Met Val  
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 Pro Pro Met Thr Thr Thr Gln Phe Leu Thr Pro Pro Ser Gln His  
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 Ser Tyr Ser Ser Ser Pro Val Asp Asn Thr Pro Ser His Gln Leu  
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 Gln Val Pro Glu Pro Thr Phe Leu Thr Pro Ser Pro Glu Ser Pro  
 2480 2485 2490  
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Ser	Thr	Pro	Cys	Lys	Asn	Ala	Gly	Thr	Cys	His	Val	Val	Asp	Arg	Arg
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Gly	Val	Ala	Asp	Tyr	Ala	Cys	Ser	Cys	Ala	Leu	Gly	Phe	Ser	Gly	Pro
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Leu	Cys	Leu	Thr	Pro	Leu	Asp	Asn	Ala	Cys	Leu	Thr	Asn	Pro	Cys	Arg
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Ser	Tyr	Ile	Cys	His	Cys	Pro	Pro	Ser	Phe	His	Gly	Pro	Thr	Cys	Arg
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His	Glu	Cys	Ala	Cys	Leu	Pro	Gly	Phe	Thr	Gly	Gln	Asn	Cys	Glu	Glu
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Val	Asp	Gly	Val	Asn	Thr	Tyr	Asn	Cys	Pro	Cys	Pro	Pro	Glu	Trp	Thr
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Cys	Val	Cys	Val	Asn	Gly	Trp	Thr	Gly	Glu	Asp	Cys	Ser	Glu	Asn	Ile
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 Arg Val Ala Ser Phe Tyr Cys Glu Cys Pro His Gly Arg Thr Gly Leu  
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 Leu Cys His Leu Asn Asp Ala Cys Ile Ser Asn Pro Cys Asn Glu Gly  
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 Ser Asn Cys Asp Thr Asn Pro Val Asn Gly Lys Ala Ile Cys Thr Cys  
 385 390 395 400  
 Pro Ser Gly Tyr Thr Gly Pro Ala Cys Ser Gln Asp Val Asp Glu Cys  
 405 410 415  
 Ser Leu Gly Ala Asn Pro Cys Glu His Ala Gly Lys Cys Ile Asn Thr  
 420 425 430  
 Leu Gly Ser Phe Glu Cys Gln Cys Leu Gln Gly Tyr Thr Gly Pro Arg  
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 Cys Glu Ile Asp Val Asn Glu Cys Val Ser Asn Pro Cys Gln Asn Asp  
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 Gly Tyr Glu Gly Val His Cys Glu Val Asn Thr Asp Glu Cys Ala Ser  
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 Gln Cys Glu Cys Pro Thr Gly Phe Thr Gly His Leu Cys Gln Tyr Asp  
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 Val Asp Glu Cys Ala Ser Thr Pro Cys Lys Asn Gly Ala Lys Cys Leu  
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 Asp Gly Pro Asn Thr Tyr Thr Cys Val Cys Thr Glu Gly Tyr Thr Gly  
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 580 585 590  
 Pro Gly Tyr Thr Gly His His Cys Glu Thr Asn Ile Asn Glu Cys Ser  
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 Ser Gln Pro Cys Arg Leu Arg Gly Thr Cys Gln Asp Pro Asp Asn Ala  
 610 615 620  
 Tyr Leu Cys Phe Cys Leu Lys Gly Thr Thr Gly Pro Asn Cys Glu Ile  
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 Asn Leu Asp Asp Cys Ala Ser Ser Pro Cys Asp Ser Gly Thr Cys Leu  
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 Asp Lys Ile Asp Gly Tyr Glu Cys Ala Cys Glu Pro Gly Tyr Thr Gly

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Lys	Asp	Met	Thr	Ser	Gly	Ile	Val	Cys	Thr	Cys	Arg	Glu	Gly	Phe	Ser																		
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785					790				795						800																		
Leu	Asn	Lys	Gly	Thr	Cys	Ile	Asp	Asp	Val	Ala	Gly	Tyr	Lys	Cys	Asn																		
				805					810																								
Cys	Leu	Leu	Pro	Tyr	Thr	Gly	Ala	Thr	Cys	Glu	Val	Val	Leu	Ala	Pro																		
			820					825						830																			
Cys	Ala	Pro	Ser	Pro	Cys	Arg	Asn	Gly	Gly	Glu	Cys	Arg	Gln	Ser	Glu																		
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Asp	Tyr	Glu	Ser	Phe	Ser	Cys	Val	Cys	Pro	Thr	Ala	Gly	Ala	Lys	Gly																		
	850					855					860																						
Gln	Thr	Cys	Glu	Val	Asp	Ile	Asn	Glu	Cys	Val	Leu	Ser	Pro	Cys	Arg																		
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Gln	Ala	Gly	Tyr	Ser	Gly	Arg	Asn	Cys	Glu	Thr	Asp	Ile	Asp	Asp	Cys																		
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 995 1000 1005  
  
 Leu Cys Pro Pro Gly Phe Thr Gly Ser Tyr Cys Gln His Val Val  
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 Asn Glu Cys Asp Ser Arg Pro Cys Leu Leu Gly Gly Thr Cys Gln  
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 Gly Pro Asn Cys Gln Asn Leu Val His Trp Cys Asp Ser Ser Pro  
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 Cys Lys Asn Gly Gly Lys Cys Trp Gln Thr His Thr Gln Tyr Arg  
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 Cys Glu Cys Pro Ser Gly Trp Thr Gly Leu Tyr Cys Asp Val Pro  
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 Ser Val Ser Cys Glu Val Ala Ala Gln Arg Gln Gly Val Asp Val  
 1100 1105 1110  
  
 Ala Arg Leu Cys Gln His Gly Gly Leu Cys Val Asp Ala Gly Asn  
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 Thr His His Cys Arg Cys Gln Ala Gly Tyr Thr Gly Ser Tyr Cys  
 1130 1135 1140  
  
 Glu Asp Leu Val Asp Glu Cys Ser Pro Ser Pro Cys Gln Asn Gly  
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 Ala Thr Cys Thr Asp Tyr Leu Gly Gly Tyr Ser Cys Lys Cys Val  
 1160 1165 1170  
  
 Ala Gly Tyr His Gly Val Asn Cys Ser Glu Glu Ile Asp Glu Cys  
 1175 1180 1185  
  
 Leu Ser His Pro Cys Gln Asn Gly Gly Thr Cys Leu Asp Leu Pro  
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 Cys Glu Ile Asn Val Asp Asp Cys Asn Pro Pro Val Asp Pro Val  
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 1235 1240 1245  
  
 Val Gly Gly Tyr Ser Cys Thr Cys Pro Pro Gly Phe Val Gly Glu  
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 1280 1285 1290  
  
 Cys Glu Cys Arg Ala Gly His Thr Gly Arg Arg Cys Glu Ser Val

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Ile Asn Gly Cys Lys Gly Lys 1310	Pro Cys Lys Asn Gly 1315	Gly Thr Cys 1320
Ala Val Ala Ser Asn Thr Ala 1325	Arg Gly Phe Ile Cys 1330	Lys Cys Pro 1335
Ala Gly Phe Glu Gly Ala Thr 1340	Cys Glu Asn Asp Ala 1345	Arg Thr Cys 1350
Gly Ser Leu Arg Cys Leu Asn 1355	Gly Gly Thr Cys Ile 1360	Ser Gly Pro 1365
Arg Ser Pro Thr Cys Leu Cys 1370	Leu Gly Pro Phe Thr 1375	Gly Pro Glu 1380
Cys Gln Phe Pro Ala Ser Ser 1385	Pro Cys Leu Gly Gly 1390	Asn Pro Cys 1395
Tyr Asn Gln Gly Thr Cys Glu 1400	Pro Thr Ser Glu Ser 1405	Pro Phe Tyr 1410
Arg Cys Leu Cys Pro Ala Lys 1415	Phe Asn Gly Leu Leu 1420	Cys His Ile 1425
Leu Asp Tyr Ser Phe Gly Gly 1430	Gly Ala Gly Arg Asp 1435	Ile Pro Pro 1440
Pro Leu Ile Glu Glu Ala Cys 1445	Glu Leu Pro Glu Cys 1450	Gln Glu Asp 1455
Ala Gly Asn Lys Val Cys Ser 1460	Leu Gln Cys Asn Asn 1465	His Ala Cys 1470
Gly Trp Asp Gly Gly Asp Cys 1475	Ser Leu Asn Phe Asn 1480	Asp Pro Trp 1485
Lys Asn Cys Thr Gln Ser Leu 1490	Gln Cys Trp Lys Tyr 1495	Phe Ser Asp 1500
Gly His Cys Asp Ser Gln Cys 1505	Asn Ser Ala Gly Cys 1510	Leu Phe Asp 1515
Gly Phe Asp Cys Gln Arg Ala 1520	Glu Gly Gln Cys Asn 1525	Pro Leu Tyr 1530
Asp Gln Tyr Cys Lys Asp His 1535	Phe Ser Asp Gly His 1540	Cys Asp Gln 1545
Gly Cys Asn Ser Ala Glu Cys 1550	Glu Trp Asp Gly Leu 1555	Asp Cys Ala 1560
Glu His Val Pro Glu Arg Leu 1565	Ala Ala Gly Thr Leu 1570	Val Val Val 1575
Val Leu Met Pro Pro Glu Gln 1580	Leu Arg Asn Ser Ser 1585	Phe His Phe 1590
Leu Arg Glu Leu Ser Arg Val 1595	Leu His Thr Asn Val 1600	Val Phe Lys 1605

Arg Asp Ala His Gly Gln Gln Met Ile Phe Pro Tyr Tyr Gly Arg  
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 Glu Glu Glu Leu Arg Lys His Pro Ile Lys Arg Ala Ala Glu Gly  
 1625 1630 1635  
 Trp Ala Ala Pro Asp Ala Leu Leu Gly Gln Val Lys Ala Ser Leu  
 1640 1645 1650  
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 Pro Met Asp Val Arg Gly Ser Ile Val Tyr Leu Glu Ile Asp Asn  
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 Arg Gln Cys Val Gln Ala Ser Ser Gln Cys Phe Gln Ser Ala Thr  
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 Asp Val Ala Ala Phe Leu Gly Ala Leu Ala Ser Leu Gly Ser Leu  
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 Pro Pro Pro Pro Ala Gln Leu His Phe Met Tyr Val Ala Ala Ala  
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 Ala Phe Val Leu Leu Phe Phe Val Gly Cys Gly Val Leu Leu Ser  
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 Arg Lys Arg Arg Xaa Gln His Gly Gln Leu Trp Phe Pro Glu Gly  
 1760 1765 1770  
 Phe Lys Val Ser Glu Ala Ser Lys Lys Lys Arg Arg Glu Xaa Leu  
 1775 1780 1785  
 Gly Glu Asp Ser Val Gly Leu Lys Pro Leu Lys Asn Ala Ser Asp  
 1790 1795 1800  
 Gly Ala Leu Met Asp Asp Asn Gln Asn Glu Trp Gly Asp Glu Asp  
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 Leu Glu Thr Lys Lys Phe Arg Phe Glu Glu Pro Val Val Leu Pro  
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 1835 1840 1845  
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 1850 1855 1860  
 Pro Gln Gly Glu Val Asp Ala Asp Cys Met Asp Val Asn Val Arg  
 1865 1870 1875  
 Gly Pro Asp Gly Phe Thr Pro Leu Met Ile Ala Ser Cys Ser Gly  
 1880 1885 1890  
 Gly Gly Leu Glu Thr Gly Asn Ser Glu Glu Glu Glu Asp Ala Pro  
 1895 1900 1905  
 Ala Val Ile Ser Asp Phe Ile Tyr Gln Gly Ala Ser Leu His Asn

1910	1915	1920
Gln Thr Asp Arg Thr Gly 1925	Glu Thr Ala Leu His 1930	Leu Ala Ala Arg 1935
Tyr Ser Arg Ser Asp Ala 1940	Ala Lys Arg Leu Leu 1945	Glu Ala Ser Ala 1950
Asp Ala Asn Ile Gln Asp 1955	Asn Met Gly Arg Thr 1960	Pro Leu His Ala 1965
Ala Val Ser Ala Asp Ala 1970	Gln Gly Val Phe Gln 1975	Ile Leu Ile Arg 1980
Asn Arg Ala Thr Asp Leu 1985	Asp Ala Arg Met His 1990	Asp Gly Thr Thr 1995
Pro Leu Ile Leu Ala Ala 2000	Arg Leu Ala Val Glu 2005	Gly Met Leu Glu 2010
Asp Leu Ile Asn Ser His 2015	Ala Asp Val Asn Ala 2020	Val Asp Asp Leu 2025
Gly Lys Ser Ala Leu His 2030	Trp Ala Ala Ala Val 2035	Asn Asn Val Asp 2040
Ala Ala Val Val Leu Leu 2045	Lys Asn Gly Ala Asn 2050	Lys Asp Met Gln 2055
Asn Asn Arg Glu Glu Thr 2060	Pro Leu Phe Leu Ala 2065	Ala Arg Glu Gly 2070
Ser Tyr Glu Thr Ala Lys 2075	Val Leu Leu Asp His 2080	Phe Ala Asn Arg 2085
Asp Ile Thr Asp His Met 2090	Asp Arg Leu Pro Arg 2095	Asp Ile Ala Gln 2100
Glu Arg Met His His Asp 2105	Ile Val Arg Leu Leu 2110	Asp Glu Tyr Asn 2115
Leu Val Arg Ser Pro Gln 2120	Leu His Gly Ala Pro 2125	Leu Gly Gly Thr 2130
Pro Thr Leu Ser Pro Pro 2135	Leu Cys Ser Pro Asn 2140	Gly Tyr Leu Gly 2145
Ser Leu Lys Pro Gly Val 2150	Gln Gly Lys Lys Val 2155	Arg Lys Pro Ser 2160
Ser Lys Gly Leu Ala Cys 2165	Gly Ser Lys Glu Ala 2170	Lys Asp Leu Lys 2175
Ala Arg Arg Lys Lys Ser 2180	Gln Asp Gly Lys Gly 2185	Cys Leu Leu Asp 2190
Ser Ser Gly Met Leu Ser 2195	Pro Val Asp Ser Leu 2200	Glu Ser Pro His 2205
Gly Tyr Leu Ser Asp Val 2210	Ala Ser Pro Pro Leu 2215	Leu Pro Ser Pro 2220

Phe Gln Gln Ser Pro Ser Val Pro Leu Asn His Leu Pro Gly Met  
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 Pro Glu Met Ala Ala Leu Gly Gly Gly Gly Arg Leu Ala Phe Glu  
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 Thr Gly Pro Pro Arg Leu Ser His Leu Pro Val Ala Ser Gly Thr  
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 2345 2350 2355  
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 Leu Ala Thr Gln Pro His Leu Val Gln Thr Gln Gln Val Gln Pro  
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Val Leu Leu Phe Phe Val Gly Cys Gly Val Leu Leu Ser Arg Lys Arg  
35 40 45

Arg Arg Gln His Gly Gln Leu Trp Phe Pro Glu Gly Phe Lys Val Ser  
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Glu Ala Ser Lys Lys Lys Arg Arg Glu Pro Leu Gly Glu Asp Ser Val  
65 70 75 80

Gly Leu Lys Pro Leu Lys Asn Ala Ser Asp Gly Ala Leu Met Asp Asp  
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Asn Gln Asn Glu Trp Gly Asp Glu Asp Leu Glu Thr Lys Lys Phe Arg  
100 105 110

Phe Glu Glu Pro Val Val Leu Pro Asp Leu Ser Asp Gln Thr Asp His  
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cgttatgaag atgaaagcct gaacctgggc gattacgttg aagatcagat tgagtctgtt 300  
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<212> PRT
<213> Artificial sequence

<220>
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<400> 17

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```

Met Asn Lys Glu Ile Leu Ala Val Val Glu Ala Val Ser Asn Glu Lys
1             5             10             15

```

```

Ala Leu Pro Arg Glu Lys Ile Phe Glu Ala Leu Glu Ser Ala Leu Ala
20             25             30

```

```

Thr Ala Thr Lys Lys Lys Tyr Glu Gln Glu Ile Asp Val Arg Val Gln
35             40             45

```

```

Ile Asp Arg Lys Ser Gly Asp Phe Asp Thr Phe Arg Arg Trp Leu Val
50             55             60

```

```

Val Asp Glu Val Thr Gln Pro Thr Lys Glu Ile Thr Leu Glu Ala Ala
65             70             75             80

```

```

Arg Tyr Glu Asp Glu Ser Leu Asn Leu Gly Asp Tyr Val Glu Asp Gln
85             90             95

```

```

Ile Glu Ser Val Thr Phe Asp Arg Ile Thr Thr Gln Thr Ala Lys Gln
100            105            110

```



Val Ile Val Gln Lys Val Arg Glu Ala Glu Arg Ala Met Val Val Asp  
115 120 125  
Gln Phe Arg Glu His Glu Gly Glu Ile Ile Thr Gly Val Val Lys Lys  
130 135 140  
Val Asn Arg Asp Asn Ile Ser Leu Asp Leu Gly Asn Asn Ala Glu Ala  
145 150 155 160  
Val Ile Leu Arg Glu Asp Met Leu Pro Arg Glu Asn Phe Arg Pro Gly  
165 170 175  
Asp Arg Val Arg Gly Val Leu Tyr Ser Val Arg Pro Glu Ala Arg Gly  
180 185 190  
Ala Gln Leu Phe Val Thr Arg Ser Lys Pro Glu Met Leu Ile Glu Leu  
195 200 205  
Phe Arg Ile Glu Val Pro Glu Ile Gly Glu Glu Val Ile Glu Ile Lys  
210 215 220  
Ala Ala Ala Arg Asp Pro Gly Ser Arg Ala Lys Ile Ala Val Lys Thr  
225 230 235 240  
Asn Asp Lys Arg Ile Asp Pro Val Gly Ala Cys Val Gly Met Arg Gly  
245 250 255  
Ala Arg Val Gln Ala Val Ser Thr Glu Leu Gly Gly Glu Arg Ile Asp  
260 265 270  
Ile Val Leu Trp Asp Asp Asn Pro Ala Gln Phe Val Ile Asn Ala Met  
275 280 285  
Ala Pro Ala Asp Val Ala Ser Ile Val Val Asp Glu Asp Lys His Thr  
290 295 300  
Met Asp Ile Ala Val Glu Ala Gly Asn Leu Ala Gln Ala Ile Gly Arg  
305 310 315 320  
Asn Gly Gln Asn Val Arg Leu Ala Ser Gln Leu Ser Gly Trp Glu Leu  
325 330 335  
Asn Val Met Thr Val Asp Asp Leu Gln Ala Lys His Gln Ala Glu Ala  
340 345 350  
His Ala Ala Ile Asp Thr Phe Thr Lys Tyr Leu Asp Ile Asp Glu Asp  
355 360 365  
Phe Ala Thr Val Leu Val Glu Glu Gly Phe Ser Thr Leu Glu Glu Leu  
370 375 380  
Ala Tyr Val Pro Met Lys Glu Leu Leu Glu Ile Glu Gly Leu Asp Glu  
385 390 395 400  
Pro Thr Val Glu Ala Leu Arg Glu Arg Ala Lys Asn Ala Leu Ala Thr  
405 410 415  
Ile Ala Gln Ala Gln Glu Glu Ser Leu Gly Asp Asn Lys Pro Ala Asp  
420 425 430  
Asp Leu Leu Asn Leu Glu Gly Val Asp Arg Asp Leu Ala Phe Lys Leu

435	440	445
Ala Ala Arg Gly Val Cys Thr	Leu Glu Asp Leu Ala Glu Gln Gly Ile	
450	455	460
Asp Asp Leu Ala Asp Ile Glu Gly Leu Thr	Asp Glu Lys Ala Gly Ala	
465	470	475
Leu Ile Met Ala Ala Arg Asn Ile Cys Trp Phe Gly Asp Glu Ala Thr		
485	490	495
Ser Gly Ser Gly His His His His His His Ser Ala Gly Lys Glu Thr		
500	505	510
Ala Ala Ala Lys Phe Glu Arg Gln His Met Asp Ser Pro Pro Pro Thr		
515	520	525
Gly Leu Val Pro Arg Gly Ser Ala Gly Ser Gly Thr Ile Asp Asp Asp		
530	535	540
Asp Lys Ser Pro Gly Ala Arg Gly Ser Glu Phe		
545	550	555